Clinical trial results:
An open-label, non-randomized study on efficacy, pharmacokinetics, pharmacodynamics, safety and tolerability of LNP023 in two patient populations with C3 glomerulopathy

Summary

EudraCT number	2017-000889-29
Trial protocol	GB ES DE FR IT
Global end of trial date	23 April 2021

Results information

Result version number	v1
This version publication date	08 May 2022
First version publication date	08 May 2022

Trial information

Trial identification

Sponsor protocol code	CLNP023X2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03832114
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, +41 8627788300, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the efficacy of LNP023 in reducing proteinuria at Week 12 (Cohort A) and to assess histopathological changes in kidney biopsies at Week 12 (Cohort B).

Protection of trial subjects:

This study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	27
EEA total number of subjects	15

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 27 patients (16 patients in Cohort A and 11 patients in Cohort B) were enrolled and treated in the treatment period 1. All 27 patients completed the study and there were no patients who discontinued the study.

Pre-assignment

Screening details:

A total of 27 patients (16 patients in Cohort A and 11 patients in Cohort B) were enrolled and treated in the treatment period 1. All 27 patients completed the study and there were no patients who discontinued the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A - no kidney transplant

Arm description:

C3G patients who have not received a kidney transplant and have reduced C3 blood levels.

Arm type	Experimental
Investigational medicinal product name	LNP023
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	Cohort B - kidney transplant

Arm description:

C3G patients who have received a kidney transplant and have C3G recurrence.

Arm type	Experimental
Investigational medicinal product name	LNP023
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg

Number of subjects in period 1	Cohort A - no kidney transplant	Cohort B - kidney transplant
Started	16	11
Completed	16	11

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A - no kidney transplant
Reporting group description:	
C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	
Reporting group title	Cohort B - kidney transplant
Reporting group description:	
C3G patients who have received a kidney transplant and have C3G recurrence.	

Reporting group values	Cohort A - no kidney transplant	Cohort B - kidney transplant	Total
Number of subjects	16	11	27
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	9	25
From 65-84 years	0	2	2
85 years and over	0	0	0
Age Continuous			
Age in Years			
Units: Years			
median	22.0	31.0	
full range (min-max)	18 to 59	18 to 70	-
Sex: Female, Male Units: Participants			
Female	6	3	9
Male	10	8	18
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska	0	1	1
Black or African American	0	1	1
White	16	9	25

Subject analysis sets	
Subject analysis set title	Cohort A
Subject analysis set type	Full analysis
Subject analysis set description:	
Summary statistics of PK parameters after multiple dose administration of LNP023 in patients in Cohorts A and B	
Subject analysis set title	Cohort B
Subject analysis set type	Full analysis

Subject analysis set description:

Summary statistics of PK parameters after multiple dose administration of LNP023 in patients in Cohorts A and B

Reporting group values	Cohort A	Cohort B	
Number of subjects	16	11	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	9	
From 65-84 years	0	2	
85 years and over	0	0	
Age Continuous			
Age in Years			
Units: Years median full range (min-max)			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Black or African American White			

End points

End points reporting groups

Reporting group title	Cohort A - no kidney transplant
Reporting group description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	
Reporting group title	Cohort B - kidney transplant
Reporting group description: C3G patients who have received a kidney transplant and have C3G recurrence.	
Subject analysis set title	Cohort A
Subject analysis set type	Full analysis
Subject analysis set description: Summary statistics of PK parameters after multiple dose administration of LNP023 in patients in Cohorts A and B	
Subject analysis set title	Cohort B
Subject analysis set type	Full analysis
Subject analysis set description: Summary statistics of PK parameters after multiple dose administration of LNP023 in patients in Cohorts A and B	

Primary: Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR)

End point title	Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR)[1]
End point description: Change in proteinuria assessed by ratio to baseline of UPCR derived from 24h urine collection	
End point type	Primary
End point timeframe: Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm comparison, therefore no comparison.

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	0[2]		
Units: g/mol				
geometric mean (confidence interval 80%)	0.55 (0.46 to 0.65)	(to)		

Notes:

[2] - This endpoint is presenting Cohort A only. Cohort B is presented in a separate table.

Statistical analyses

No statistical analyses for this end point

Primary: Cohort B: Change from baseline in C3 Deposit

End point title	Cohort B: Change from baseline in C3 Deposit[3]

End point description:

Histopathological changes in kidney biopsies as assessed by change from baseline in C3 Deposit Score (based on immunofluorescence microscopy)

End point type	Primary

End point timeframe:

Week 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm comparison, therefore no comparison.

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	7		
Units: Percentage				
median (confidence interval 80%)	(to)	-2.50 (-3.75 to -0.75)		

Notes:

[4] - This endpoint is presenting Cohort B only. Cohort A is presented in a separate table.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR)

End point title	Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR)

End point description:

Ratio to baseline UPCR derived from 24 hour urine collection

End point type	Secondary

End point timeframe:

Week 12: Day 84

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: 24 hr g/mol				
geometric mean (confidence interval 80%)	0.55 (0.46 to 0.65)	0.79 (0.49 to 1.28)		

Statistical analyses

Statistical analysis title	Cohort A

Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.55
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.46
upper limit	0.65

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4766
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.79
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.49
upper limit	1.28

Statistical analysis title	Overall Analysis
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed Model of Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.59

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.51
upper limit	0.69

Secondary: Change from baseline in Urine Protein (UP) Excretion

End point title	Change from baseline in Urine Protein (UP) Excretion
End point description:	
Ratio to baseline UP excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: 24 h mg/day				
geometric mean (confidence interval 80%)	0.57 (0.47 to 0.68)	1.00 (0.75 to 1.33)		

Statistical analyses

Statistical analysis title	Overall Analysis
Statistical analysis description:	
Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0011
Method	Mixed Model Repeated Measures (MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.57
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.68

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9998
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	1.33

Statistical analysis title	Overall Study
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0016
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.66
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.56
upper limit	0.77

Secondary: Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion

End point title	Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion
End point description: Ratio to baseline UACR excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe: Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: 24 hr g/mol				
geometric mean (confidence interval 80%)	0.55 (0.47 to 0.64)	0.61 (0.30 to 1.27)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.55
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.64

Statistical analysis title	Overall Study
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.51
upper limit	0.71

Statistical analysis title	Cohort B
Statistical analysis description:	
Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3707
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.61
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.3
upper limit	1.27

Secondary: Change from baseline change in Urinary Albumin (UA) Excretion

End point title	Change from baseline change in Urinary Albumin (UA) Excretion
End point description:	
Ratio to baseline UA excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: 24 h mg/day				
geometric mean (confidence interval 80%)	0.57 (0.47 to 0.70)	0.81 (0.67 to 0.98)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description:	
Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0018
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.57
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.7

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1632
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.81
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.67
upper limit	0.98

Statistical analysis title	Overall Study
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Mixed Model Repeated Measure (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.57
upper limit	0.79

Secondary: Change from baseline in estimated glomerular filtration rate (eGFR)	
End point title	Change from baseline in estimated glomerular filtration rate (eGFR)
End point description: Effect of LNP023 on estimated glomerular filtration rate (eGFR)	
End point type	Secondary
End point timeframe: Day 7, Day 28, Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: ml/min				
arithmetic mean (confidence interval 80%)	2.59 (0.12 to 5.06)	-0.61 (-3.36 to 2.15)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1795
Method	Mixed Model of Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	2.59
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.12
upper limit	5.06

Statistical analysis title	Overall
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3754
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.32
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.59
upper limit	3.22

Statistical analysis title	Cohort B
Statistical analysis description:	
Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7763
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-0.61
Confidence interval	
level	Other: 0.78 %
sides	2-sided
lower limit	-3.36
upper limit	2.15

Secondary: Change from baseline in serum creatinine	
End point title	Change from baseline in serum creatinine
End point description:	
The effect of LNP023 on renal function - serum creatinine	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: mmol/L				
arithmetic mean (confidence interval 80%)	-5.04 (-9.36 to -0.72)	7.17 (-1.79 to 16.13)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1364
Method	Mixed Model Repeated Measuers (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-5.04
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-9.36
upper limit	-0.72

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3038
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	7.17
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.79
upper limit	16.13

Statistical analysis title	Overall
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8352
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-0.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-5.56
upper limit	4.01

Secondary: Change from baseline in creatinine clearance

End point title	Change from baseline in creatinine clearance
End point description: The effect of LNP023 on renal function - creatinine clearance	
End point type	Secondary
End point timeframe: Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	8		
Units: mL/min				
geometric mean (confidence interval 80%)	1.07 (0.99 to 1.17)	1.20 (0.83 to 1.72)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2752
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.07
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.99
upper limit	1.17

Statistical analysis title	Overall
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1963
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1
upper limit	1.2

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.476
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.83
upper limit	1.72

Secondary: Change from baseline and evolution of hematuria

End point title	Change from baseline and evolution of hematuria
End point description:	
The effect of LNP023 on renal function - hematuria	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: rbc/hpf				
Week 12: Day 84: <9 rbc/hpf n (%)	10	3		
Week 12: Day 84: >= 9 to =<50 rbc/hpf n (%)	0	0		
Week 12: Day 84: >50 rbc/hpf n (%)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void

End point title	Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void
End point description:	
Ratio to baseline of UPCR reduction derived from total cumulative urinary excretion first morning void	
End point type	Secondary
End point timeframe:	
Week 9: Day 64	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	7		
Units: g/mol				
geometric mean (confidence interval 80%)	0.56 (0.48 to 0.65)	0.99 (0.76 to 1.28)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.56
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.48
upper limit	0.65

Statistical analysis title	Overall Analysis
Statistical analysis description: Overall- Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.64
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.56
upper limit	0.72

Statistical analysis title	Cohort B
Statistical analysis description: Day 64	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9544
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	1.28

Secondary: Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void

End point title	Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void
End point description:	
UACR reduction derived from total cumulative urinary excretion first morning void	
End point type	Secondary
End point timeframe:	
Week 9: Day 64	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	7		
Units: g/mol				
geometric mean (confidence interval 80%)	0.59 (0.50 to 0.69)	0.87 (0.60 to 1.26)		

Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description:	
Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.59

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.5
upper limit	0.69

Statistical analysis title	Cohort B
Statistical analysis description:	
Day 64	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6209
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Median difference (final values)
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.6
upper limit	1.26

Statistical analysis title	Overall Analysis
Statistical analysis description:	
Overall- Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.63
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.54
upper limit	0.73

Secondary: Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC)

End point title	Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC)

End point description:

Plasma: Non-compartmental parameter analysis related to total drug for the area under the plasma-concentration-time curve calculated from time.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4

End point values	Cohort A	Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	11		
Units: hr*ng/mL				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC)

End point title	Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC)

End point description:

Plasma: Non-compartmental parameter analysis related to total drug for the area under the plasma-concentration-time curve calculated to the end of the dosing interval (ngxh/mL).
Data will be provided at at later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4

End point values	Cohort A	Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	11		
Units: hr*ng/mL				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed maximum concentration after drug administration (Cmax)

End point title	Observed maximum concentration after drug administration

	(Cmax)

End point description:

Plasma: Non-compartmental parameter analysis related to total drug, including but not limited to Cmax after the first dose.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4

End point values	Cohort A	Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	11		
Units: ng/ML				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed mimum concentration after drug administration (Ctrough)

End point title	Observed mimum concentration after drug administration (Ctrough)

End point description:

Plasma: Non-compartmental parameter analysis related to total drug, including but not limited to Ctrough (Cmin) after the first dose.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4

End point values	Cohort A	Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	11		
Units: ng/mL				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach the maximum plasma concentration (Tmax)

End point title	Time to reach the maximum plasma concentration (Tmax)

End point description:

Plasma: Non-compartmental parameter analysis related to total drug, including but not limited to Tmax after the first dose.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	11		
Units: hour (hr)				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline Complement C3 biomarker in serum

End point title	Summary of Change from Baseline Complement C3 biomarker in serum

End point description:

To assess the effect of LNP023 on alternative complement pathway hyperactivity.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 12

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	10		
Units: g/L				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to baseline summary of Plasma Bb in blood and urine

End point title	Ratio to baseline summary of Plasma Bb in blood and urine

End point description:

To assess the relationship between LNP023 dose and pharmacodynamic biomarker levels of blood Bb in blood and urine.
Data will be provided at a later date.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4 and 12

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	10		
Units: ng/mL				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events	
Adverse event reporting additional description:	
Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Cohort A - Run-in Phase
Reporting group description:	
Cohort A - Run-in Phase	
Reporting group title	Cohort A - Dose Escalation Phase
Reporting group description:	
Cohort A - Dose Escalation Phase	
Reporting group title	Cohort B - Dose Escalation Phase
Reporting group description:	
Cohort B - Dose Escalation Phase	
Reporting group title	Cohort B - Run-in Phase
Reporting group description:	
Cohort B - Run-in Phase	
Reporting group title	Cohort B - LNP023 200mg b.i.d.
Reporting group description:	
Cohort B - LNP023 200mg b.i.d.	
Reporting group title	Cohort A - LNP023 200mg b.i.d.
Reporting group description:	
Cohort A - LNP023 200mg b.i.d.	

Serious adverse events	Cohort A - Run-in Phase	Cohort A - Dose Escalation Phase	Cohort B - Dose Escalation Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort B - Run-in Phase	Cohort B - LNP023 200mg b.i.d.	Cohort A - LNP023 200mg b.i.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort A - Run-in Phase	Cohort A - Dose Escalation Phase	Cohort B - Dose Escalation Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	6 / 16 (37.50%)	5 / 11 (45.45%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Spider vein			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Intentional self-injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood luteinising hormone increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Anosmia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Migraine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Skin discolouration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory tract infection viral			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort B - Run-in Phase	Cohort B - LNP023 200mg b.i.d.	Cohort A - LNP023 200mg b.i.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	6 / 11 (54.55%)	8 / 16 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Spider vein			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Intentional self-injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Blood luteinising hormone increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			

Anosmia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vomiting			

subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Skin discolouration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			

subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Iron deficiency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2018	Non-Substantial Amendment: text added to indicate patients must receive vaccinations against N. meningitidis, S. pneumoniae and H. influenzae prior to first dosing.
22 February 2019	Germany: The purpose of this local protocol amendment was to modify the study stopping rules for drug related events and to clarify if the study was halted the restart would be documented by a substantial amendment as per Health Authority questions.
20 August 2019	The purpose of this amendment was to include a second treatment period (Treatment period 2) to enable the prolongation of treatment by 12 weeks for any patient.
07 February 2020	The purpose of this amendment was mainly to correct the estimation of the blood sample volume to be collected, confirming that there is no increased risk for the patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported